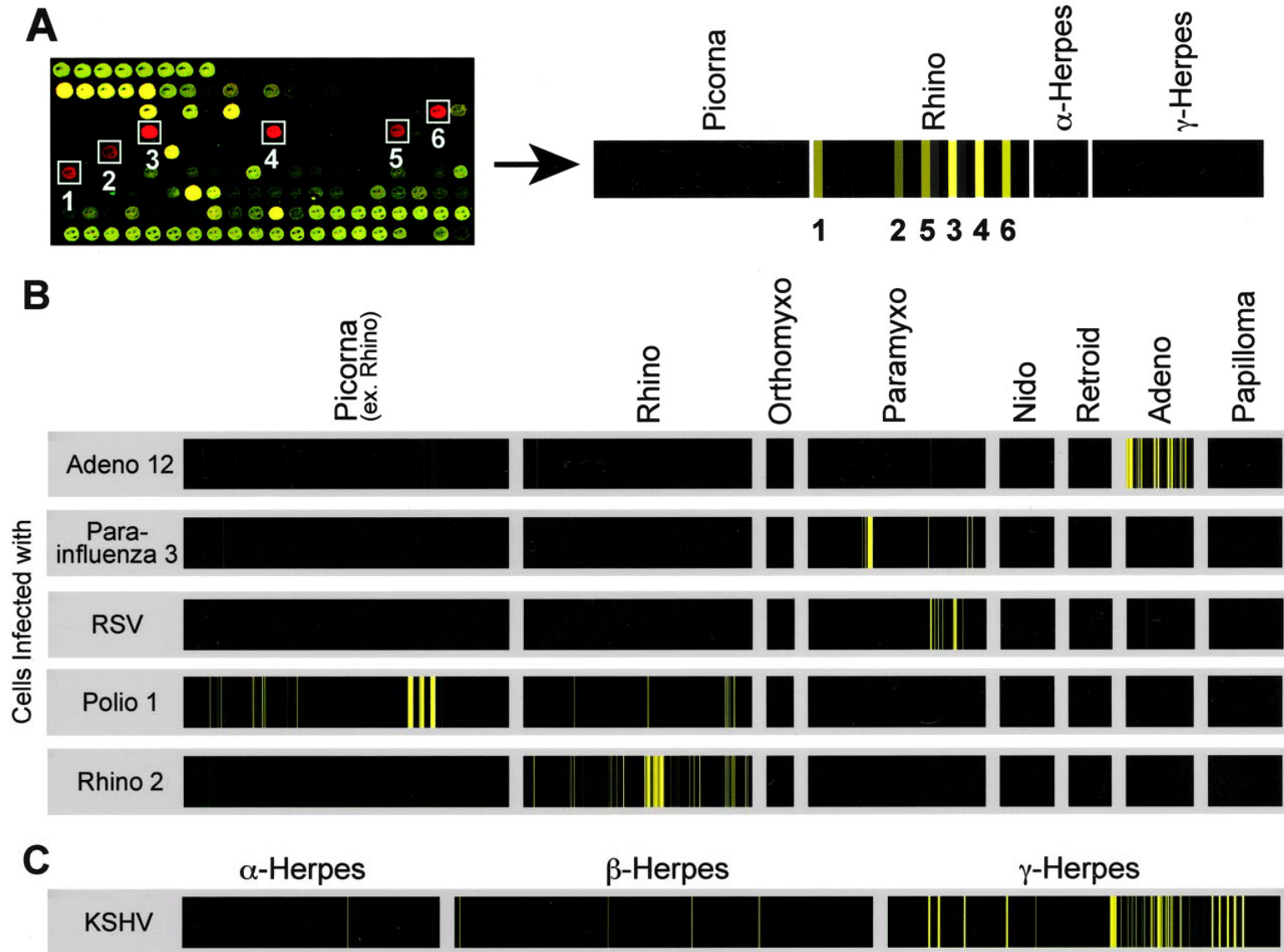


# Novel Approaches to Detection of Adventitious Agents

Peter Wright

#1 Detection of known (or unknown)  
viruses by microarray after PCR  
amplification using random degenerate  
primers\*

\* Wang D et al. PNAS  
99:15687,2002



Wang, David et al. (2002) Proc. Natl. Acad. Sci. USA 99, 15687-15692

# Comments of Don Ganem

- Had not thought of this application but intrigued.
- Concerned that the tool is still an academic research tool without validation or standardization
- Because of amplification they recognize possibility of contamination.
- Would not yet feel comfortable with a definitive yes or no re adventitious agents.
- To date used in detecting viruses in tissue culture and in nasal secretions

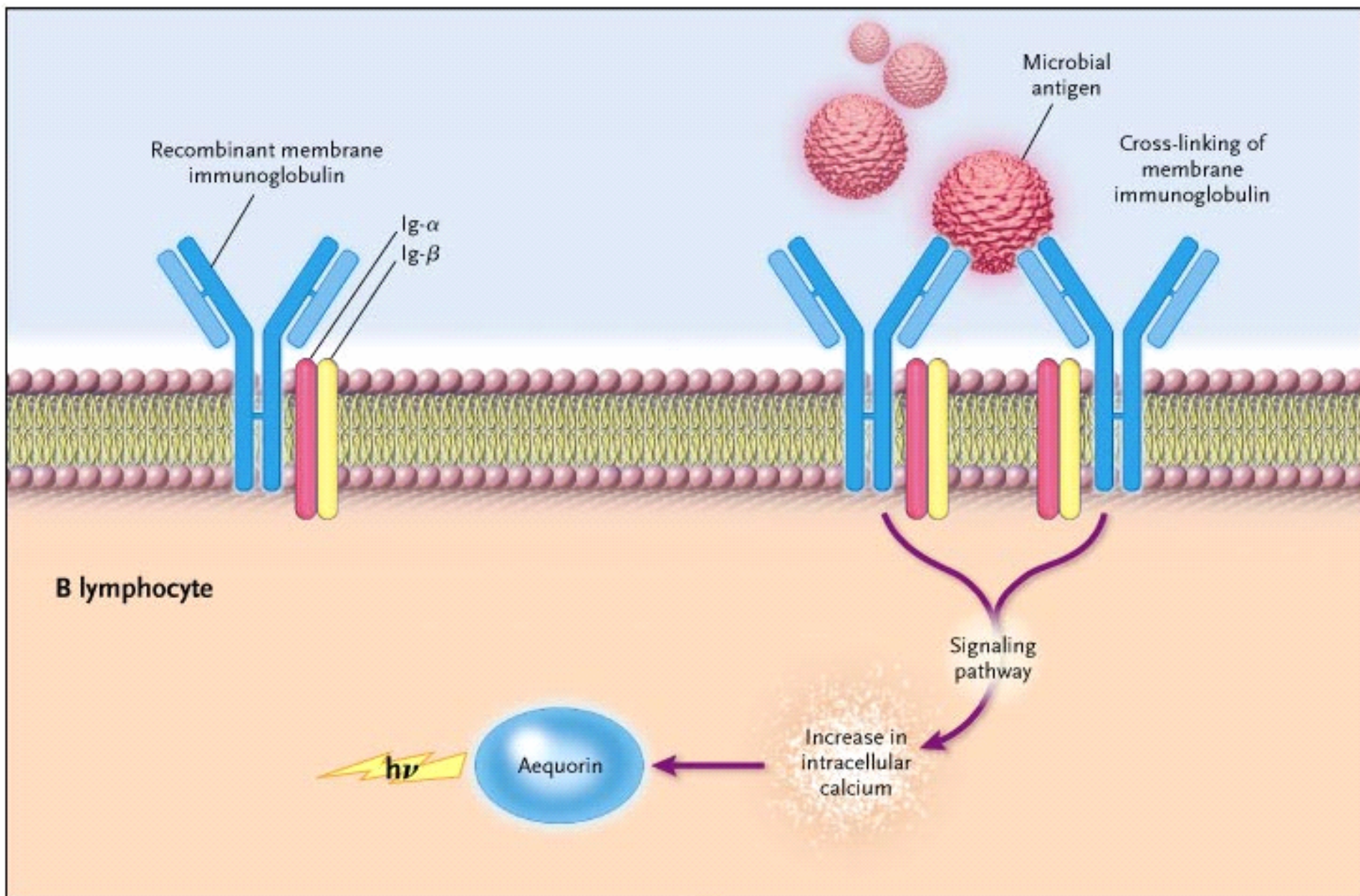
## Comments of Don Ganem, cont.

- Approach is being industrialized by others, e.g. Genome Institute of Singapore
- He did not feel that his laboratory was prepared to take on this task but would be happy to see the application develop
- There is not patent protection in this area that he is aware of

## #2 B-Cell based Sensors\*

- *Comments in David Relman's Shedding Light on Microbial Detection. NEJM 349:2162, 2003.*
- Antibody based detection system for anthrax and E. coli in which lymphocyte expressing a specific antibody is engineered to produce aequorin when the antibody signaling pathway leads to an increase intracellular calcium

\*Rider TH, et al. Science 301:213-, 2003



# #3 Perturbation of the innate immune response by infecting organism\*

- Hypothesis -The resting profile of the cell may be altered by adventitious agents and there may be signatures of infecting organisms
- Presently as with other assays discussed is in developmental stages
- Much currently aimed at lymphoid cell responses but could be adapted to tissue culture ( did not have a chance to talk directly with Dr. Relman).

\*Relman DA, JID 186(suppl 2) S524-, 2002

## Pathogens as source of signature

- Broad range PCR
- Microbial/viral survey (phyloarray)
- Subtractive/comparative methods
  - representational difference analysis
  - differential display
- Expression or phage display library screening (using host antisera or T-cells)
- Small molecule or protein detection (e.g. with mass Spectroscopy)

## Host as source of signature

- Host genome-wide transcript profiling (e.g. using microarrays)
- Host protein profiling (e.g. using microarrays, or mass spectroscopy)

Relman et al. J Infect Dis. 2002 Dec 1;186 Suppl 2:S254-8.

## #4 Nanotechnology

Not really prepared to speak about this but is clearly part of the broader scientific and biodefense agenda that will bring us to a new generation of sensors for adventitious agents. Somehow we have to stay abreast and take advantage of these new technologies recognizing that the individual academic laboratories will not develop the capacity and special skills necessary to satisfy regulatory requirements.